

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
176 tcttgacgttccccggcggtccccgtgcgt	o
177 tctgtgcgtcctgtgcgtcctgtgcgt	o
178 tctggcggggaagt	o
179 tctgaggttgaagt	o
180 tctgacgttgaagt	o
181 tctagcgttgaagt	o
182 tccagacgttgaagt	o
183 tctgacggggaagt	o
184 tctggcggtgaagt	o
185 ggctccggggagggaattttgtctat	o
186 atagacaaaaattccccccggagcc	o
187 tccatgagcttcttgagtct	rna
188 tctgcgtgtctccgcttctt	so
189 <del>tctgcgtgtctccgcttctt</del> <i>regtcgcgttcgcttctt</i>	s20
190 tctgagcattgcacatcatctg	o
191 cagatttgtcaatgtctcga	o
192 tccatgtcgttctctgatgcg	o
193 gcgatgtcgttctctgatgct	o
194 gcgatgtcgttctctgatgcg	o
195 tccatgtcgttccgcgcgcg	o
196 tccatgtcgttctctgcgcgt	o
197 tccatgtcgttctctgtagct	o
198 gcggcgggcggcgcgcgcgc	o
199 atcaggaaacgtcatgggaagc	o
200 tccatgagcttctctgagtct	p-ethoxy
201 tcaacgtt	p-ethoxy
202 tcaagctt	p-ethoxy
203 tctgtcgttctctgtcgtt	s
204 tccatgtcgtttttgtcgtt	s
205 tctgtcgttctctgtcgtt	s
206 tctgtcgttctctgtcgtt	s
207 btccattccatgacgttctctgatctcca	os
208 tctgtcgtttttgtcgtt	s
209 tctgcgtgtctccgcttctt	s
210 tctgcgtgtctccgcttctt	s
211 tctgcgtgttgcgttctt	s
212 tctgtcgttctctgcgttggaaacgacagg	o
213 tctgtcgttctctgcgtttcaacgtcaggaaacgacagga	o
214 ggggtctgcgttttgggggg	sos
215 ggggtctgcgttttgggggg	sos
216 tccggccgttgaagt	o
217 tccggacgttgaagt	o
218 tccggccgttgaagt	o
219 tccagacgttgaagt	o
220 tccggacgttgaagt	o
221 tccagacgttgaagt	o
222 tccatgtzgttctctgtzgtt	s
223 tccatgacgttctctgacgtt	sos
224 ggggttgacgttttgggggg	sos
225 tccaggacttctctcaggtt	s
226 ttttttttttttttttttt	s
227 tccatgccgttctctgccgtt	s
228 tccatggcgggcctggcggg	s
229 tccatgacgttctctgccgtt	s
230 tccatgacgttctctggcggg	s
231 tccatgacgttctctgccgtt	s
232 tccatgacgttctctgacgtt	s
233 tccatgcgttgcgttgcgtt	s
234 tccatgcgttgcgttgcgtt	s
235 btccattccattctagccctgagcttccat	os
236 tccatgacgttctctgacgtt	o
237 tccatgtcgttctctgtcgtt	o
238 tccatgacgttctctgacgtt	o
239 tccattgcgttctctgcgtt	o
240 tccatgacgttctctgacgtt	o
241 tccatgatttctctgcgttctctgattt	o
242 tccatgacgttctctgacgttctctgacgtt	s
243 ggcggcg <del>ggcgggcggg</del> <i>g</i>	o
244 tccagacgttctctgacgtt	s
245 tctgcgttgcgttgcgtt	s
246 tctgcgttgcgttgcgtt	s
247 tctgcgttgcgttgcgtt	s
248 gcgtgcgttgcgttgcgtt	s
249 czggczggczggczggczgg	o

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
250 ggggggggggggggggggggg	S
251 agicccgigaacgiattcac	O
252 tgcgtttgctgcttgcgtt	S
253 tgcgtttgctgcttgcgtt	S
254 tgcgtttgctgcttgcgtt	S
255 tgcgtttgctgcttgcgtt	S
256 tgcgtttgctgcttgcgtt	S
257 cccccccccccccccccccc	S
258 tctagcgttttttagcgttcc	SOS
259 tgcacccccagggccaccat	S
260 tgcgtcgtcgtcgtcgtcgtt	SOS
261 tgcgtcgttgcgttgcgtt	SOS
262 tgcgtcgtttgcgttttgcgtt	SOS
263 tgcgtcgttgcgttttgcgtt	SOS
264 ggggagggaggaacttcttaaaattccccagaatgttt	O
265 aaacattctgggggaattttaagaagtctctccctcccc	O
266 atgtttacttcttaaaattccccagaatgttt	O
267 aaacattctgggggaattttaagaagttaaacat	O
268 atgtttactagacaaaattccccagaatgttt	O
269 aaacattctgggggaattttgtctagtaaacat	O
270 aaaaattgacgtttttaaaaa	SOS
271 ccccttgacgttttcccccc	SOS
272 ttttcgttgttttgcgtt	
273 tgcgtcgttttgcgttttgcgtt	SOS
274 ctgcagccctgggac	O
275 acccgtcgttaattatagtaaaacc	O
276 ggtacctgtggggacattgtg	O
277 agcaccgaacgtgagagg	O
278 tccatgccgttctctccgtt	O
279 tccatgacggtcctgaggg	O
280 tccatgccggtcctgaggg	O
281 tccatgacggtcctgaggg	O
282 ctggtctttctggttttttctgg	S
283 tcagggtggggggaacctt	SOS
284 tccatgaggttctctagttct	O
285 tccatgatgttctctagttct	O
286 cccgaagtcatctctcttaaacctgg	O
287 ccagggttaagaggaaatgaactcggg	O
288 tccctggzggggaagt	O
289 gzzggzgggzzggzggzggc	X
290 tccatgtgcttctctgatgct	O
291 tccatgtccttctctgatgct	
292 tccatgtcgttctctagttct	
293 tccaaagttagttctctagttct	O
294 tccatgtagttctctagttct	O
295 tcccgcgcgttccgcgcgtt	S
296 tccctggcgggtcctggcgggt	S
297 tccctggaggggaagt	O
298 tccctgggggggaagt	O
299 tccctggtggggaagt	O
300 tgcgtcgtttgcgttttgcgtt	O
301 ctggtctttctggttttttctgg	O
302 tccatgacgttctctgacgtt	
303 tccaggacttctctcaggtt	SOS
304 tzgtzgtttgtzgtttgtzgtt	O
305 bctgctgcttctgcttttgcgtttttt	OS
306 gctatgacgttccaagg	S
307 tcaacgtt	S
308 tccaggacttctctcaggtt	O
309 ctctctgtaggcccgcttg	S
310 ctctcgttggaccctctgg	S
311 gtccgggccaaggccaaagtc	S
312 gtgcgcgcgagccgaaatc	S
313 tccatgaigtctctgaigt	S
314 aatagtcgcatacaaaaac	O
315 aatagtcgcacatggcggggc	O
316 btttttccatgtcgttctctgatgctttt	OS
317 tccctgcttgaagttttt	O
318 gctagcttttagagcttttagagctt	O
319 tgcgtccttcccccctccc	O
320 tgcagcttcccccctccc	O
321 tgcgtccttcccccctccc	O
322 tgcgtccttcccccctccc	O
323 tgcagcttcccccctccc	O

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
324 tcgtcgatccccccccccc	o
325 tcctgacgttgaagt	s
326 tcctgccgttgaagt	s
327 tcctgacgttgaagt	s
328 tctgagcttgaagt	s
329 tcctggcggggaagt	s
330 aaaaatctgtgttttataaaaa	sos
331 gatccagtcacagtgacctggcagaatctggat	o
332 gatccagattctgccaggtcactgtgactggat	o
333 gatccagtcacagtgactcagaagaatctggat	o
334 gatccagattctgtcagtcactgtgactggat	o
335 tcgtcggtccccccccccc	o
336 tzgtggtccccccccccc	o
337 tzgtcggtccccccccccc	o
338 tcgtzgttccccccccccc	o
339 tcgtcgctccccccccccc	o
340 tcgtcgttccccccccccc	o
341 tcggcgttccccccccccc	o
342 ggccctttccccccccccc	o
343 tcgtcggtttgacgttttgcgtt	s
344 tcgtcggtttgacgttttgcgtt	s
345 ccgtcggtccccccccccc	o
346 gcgtcggtccccccccccc	o
347 tcgtcattccccccccccc	o
348 acgtcggtccccccccccc	o
349 ctgctggtccccccccccc	o
350 btttttcgtcggtccccccccccc	os
351 tcgtcggtcccccccccccb	o
352 tcgtcggtttgtcggtttgtcggtb	o
353 tccagttccttcctcagtc	o
354 tzgtcggtttgtcggtttgtcggt	o
355 tcctggaggggaagt	s
356 tcctgaaaagggaagt	s
357 tcgtcggtccccccccccc	s
358 tzgtzgtttgtzgtttgtzgtt	s
359 ggggtcaagcttgagggggg	sos
360 tgctgcttccccccccccc	s
361 tcgtcggtcggtt	s2
362 tcgtcggtcggtt	s20
363 tcgtcggtcggtt	os2
364 tcaacgttga	s
365 tcaacgtt	s
366 atagttttccatttttttac	
367 aatagtcgccatcgcgcgac	o
368 aatagtcgccatccccggac	o
369 aatagtcgccatccccccc	o
370 tgctgctttgtgcttttgcgtt	o
371 ctgtgctttctgtgttttctgtg	s
372 ctaatctttctaatttttttctaa	s
373 tcgtcggttggtgtcggttggtcggt	s
374 tcgtcggttggtgtcggttttggt	s
375 accatggacgagctgtttccctc	
376 tcgtcggtttgcgtgcgttt	s
377 ctgttaagtgaagcttgagag	
378 gagaacgctggaccttc	
379 cgggcgactcagtcctatcgg	
380 gttctcagataaagcggaaccagcaacagacacagaa	
381 ttctgtgtcgtttgtcgttccgctttatctgagaac	
382 cagacacagaagcccgatagacg	
383 agacagacacgaacgaccg	s
384 gtctgtcccatgatctcgaa	
385 gctggccagcttacctcccg	
386 ggggcctctatacaacctggg	
387 ggggtccctgagactgcc	
388 gagaacgctggaccttcct	
389 tccatgtcggctcctgatgct	
390 ctcttgccacctggaaggta	
391 aggtacagccaggactacga	
392 accatggacgactgtttccctc	
393 accatggattacctttttccctt	
394 atggaagggtccagcgttctc	o
395 agcatcaggaccgacatgga	o
396 ctctccaagctcacttacag	
397 tcctgagactgccccacctt	

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
471 tcagctctgggtactttttca	
472 tgggttacgggtctgtcccatg	
473 gtctatcggaggactggcg	
474 ctttttacgggaggcg	
475 gaggggacattttacggg	
476 tgtccagccgaggggacat	
477 cgggcttacggcgatgctg	
478 tggaccttctatgtcggtcc	
479 tgtcccatgtttttagaage	
480 gtgggttacgggtcgtgccc	
481 cctccaaatgaagaccccc	
482 ttgtactctccatgatggtt	
483 ttccatgctgtccggctgg	
484 gaccttctatgtcggtcctg	
485 gagaccgctcgaccttcgat	
486 ttgccccatatttttagaaac	
487 ttgaaactgaggtgggac	
488 ctatcggaggactggcgccg	
489 cttggagggtcccccggcg	
490 gctgaaccttccatgctgtt	
491 tagaaacagcattctcttttagggcagcaca	
492 agatgggttctcagataaagcgga	
493 ttccgctttatctgagaaccatct	
494 gtcccagggtgtatagagctgc	
495 gcgccagtcctccgatagac	
496 atcggaggactggcgccg	
497 ggtctgtcccatatttttag	SOS
498 ttttcaacgttgagggggg	SOS
499 †ttttcaacgttgattttt	SOS
500 ggggtcaacgttgattttt	SOS
501 ggggttttcaacgttttgagggggg	SOS SOS
502 ggttacgggtctgtcccatat	
503 ctgtcccatatttttagaca	
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505 cgtctatcgggttctgtgtctg	
506 ggccatcccacattgaaagt	
507 ccaaatatcggttggtcaagcac	
508 gtgcttgaccaccgatatttg	
509 gtgctgatcccgatatcctgttcgg	
510 ggccaaactttcaatgtgggatggctc	
511 ttccgcccgaatggcctcaggatggtac	
512 tatagtccctgagactgccccaccttctcaacaacc	
513 gcagcctctatacaacctgggacggga	
514 ctatcggaggactggcgccg	
515 tatcggaggactggcgccg	
516 gatcggaggactggcgccg	
517 ccgaacaggatcgggtgatcagcac	
518 ttttgggtcaacgttgagggggg	
519 ggggtcaacgttgagggggg	SOS
520 cgccgcgcgcgcgcgcgcg	S
521 ggggcatgacgttcgggggg	SS
522 ggggcatgacgttcaaaaaa	S
523 ggggcatgacgttcgggggg	S
524 ggggcatgacgttcgggggg	SOS
525 aaaaacatgacgttcaaaaaa	SOS
526 aaaaacatgacgttcgggggg	SOS
527 ggggcatgacgttcaaaaaa	SOS
528 accatggagcatctgtttcccctc	S
529 gccatggagcaactgtttcccctc	S
530 ccccccccccccccccc	SOS
531 gggggggggggggggggg	SOS
532 gctgtaaaatgaatcgccg	SOS
533 ttccggcggaactcctccatt	SOS
534 tatgcgcgcgggacttat	SOS
535 ggggtaatcgatcagggggg	SOS
536 tttgagaacgtggaccttc	SOS
537 gatcgtgatctaagtctcg	SOS
538 gtcggtcctgatgctgttc	SOS
539 tcgtcgtcagttcgtgtcg	SOS
540 ctggaccttccatgtcgg	SOS
541 gctcgttcagcgctct	SOS
542 ctggaccttccatgtc	SOS
543 caactgtccttcgtcga	SOS
544 cgtggaccttccatgtcgg	SOS

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
545 gctgagctcatgccgtctgc	sos
546 aacgctggacattccatgtc	sos
547 tgcattgccgtacacagctct	sos
548 ccttccatgtcggctcctgat	sos
549 tactcttcggatcccttgcg	sos
550 ttccatgtcggctcctgat	sos
551 ctgattgctctctcgtga	sos
552 gggcgcttatcctgactgcc	o
553 cctacgttgatgcgcccagct	o
554 ggggtaatcgatgagggggg	o
555 ttccggcggactcctccatt	o
556 ttttttttttttttttttt	o
557 gggggtttttttttggggg	o
558 tttttgggggggggttttt	o
559 ggggggggggggggggggt	o
560 aaaaaaaaaaaaaaaaaaaa	o
561 cccccccccccccccccc	o
562 aaaaacccccccccccaaa	o
563 ttgaaattcaggactggtaggtgag	o
564 ttgaaattcctcagcgtctccagtggc	o
565 aattctctatcggggcttctgtgtctgttgcgttccgctttat	o
566 ctagataaagcggaaccagcaacagacacagaagccccgatagag	o
567 tttctagagaggtgcacaatgctctgg	o
568 ttgaaattcctgtgtacagaagcgagaagc	o
569 ttgcccgcgttagacttaa <sup>g</sup> ctgagagata <sup>e</sup>	o
570 ttggggccacgagagacagagacacttc	o
571 ttggggcccgcttctcgtctctgtacacg	o
572 gagaacgctggaccttccat	s
573 tccatgtcggctcctgatgct	s
574 ctgtcg	s
575 tcgtga	s
576 cgtcga	s
577 agtgct	s
578 ctgtcg	o
579 agtgct	o
580 cgtcga	o
581 tcgtga	o
582 gagaacgctccagcttcgat	o
583 gctagacgtaagcgtga	o
584 gagaacgctcgaccttccat	o
585 gagaacgctggacctatccat	o
586 gctagagggttagcgtga	o
587 gagaacgctggaccttccat	o
588 tcacgctaacgtcttagc	o
589 bgctagacgttagcgtga	o
590 atggaaaggtcagcgttctc	o
591 gagaacgctggaccttcgat	o
592 gagaacgatggaccttccat	o
593 gagaacgctggaccttccat	o
594 gagaacgctccagcactgat	o
595 tccatgtcggctcctgctgat	o
596 atgtcctcggctcctgatgct	o
597 gagaacgctccaccttccat	o
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600 tcctga	o
601 tcaacgtt	o
602 aacgtt	o
603 aacgttga	o
604 tcacgctaacctcttagc	o
605 gagaacgctggaccttgcat	o
606 gctggaccttccat	o
607 gagaacgctggaccttccat	o
608 gagaacgctggaccttccat	o
609 aacgttgaggggcat	o
610 atgccccctcaacgtt	o
611 tcaacgttga	o
612 gctggaccttccat	o
613 caacgtt	o
614 acaacgttga	o
615 tcacgt	o
616 tcaacgtt	o
617 tcgtca	o
618 aggatatac	o

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
619 tagacgtc	o
620 gacgtcat	o
621 ccatgcat	o
622 atcgatgt	o
623 atgcatgt	o
624 ccatgcat	o
625 agcgctga	o
626 tcagcgat	o
627 ccttcgat	o
628 gtgccgggggtctccgggc	o
629 gctgtggggcggtccctg	s
630 btcaacggt	o
631 ftcaacggt	o
632 faacgttga	o
633 tcaacgt	s
634 aacgttg	s
635 cgacga	o
636 tcaacggt	o
637 tcgga	o
638 agaacggt	o
639 tcatcgat	o
640 taaacggt	s
641 ccaacggt	s
642 gctcga	s
643 cgacgt	s
644 cgtcgt	s
645 acgtgt	s
646 cgttcg	s
647 gagcaagctggaccttccat	s
648 cgcgta	s
649 cgtacg	s
650 tcaccggt	s
651 caagagatgctaacaatgca	s
652 acccatcaatagctctgtgc	s
653 ccattcgat	o
654 tcgacgtc	o
655 ctacgcgt	o
656 taagcgct	o
657 tcgcgaattcgcg	o
658 atggaaaggtccagcgttct	o
659 actggacggttagcgtga	o
660 cgcctggggctggtctgg	o
661 gtgtcgggggtctccgggc	o
662 gtgccgggggtctccgggc	o
663 cgcctgcggcggtgttg	o
664 gaagttcacgttgaggggcatt	o
665 atctggtgagggcaagctatg	s
666 gttgaaacccgagaacatcat	s
667 gcaacggt	o
668 gtaacggt	o
669 cgaacggt	o
670 gaaacggt	o
671 caaacggt	o
672 ctaacggt	o
673 ggaaggtt	o
674 tgaacggt	o
675 acaacggt	o
676 ttaacggt	o
677 aaaacggt	o
678 ataacggt	o
679 aacgttct	o
680 tccgatcg	o
681 tccgtacg	o
682 gctagacgctagcgtga	o
683 gagaacggtggttctcatccat	o
684 gagaacggttagaccttctat	o
685 actagacggttagtgtga	o
686 cacaccttggtcaatgtcacgt	o
687 tctccatcctatgggttttatcg	o
688 cgctggaacctccat	o
689 caccaccttggtcaatgtcacgt	o
690 gctagacggttagctgga	o
691 agtgcgattgcagatcg	o
692 ttttcgttttgtggttttgtggtt	o

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
693 ttttcgtttgtcgttttgtcggt	
694 tttttgtttgtgggtttgtgggt	
695 accgcatggattcttaggcca	s
696 gctagacgttagcgt	o
697 aacgctggaccttccat	o
698 tcaazgtt	o
699 ctttcgat	o
700 actagacgttagtgtga	s
701 gctagaggttagcgtga	s
702 atggactctccagcgttctc	o
703 atcgactctcgagcgttctc	o
704 gctagacgttagc	o
705 gctagacgt	o
706 agtgcgattcgagatcg	o
707 tcagzgt	o
708 ctgattgctctctcgtga	o
709 tzaacgtt	o
710 gagaazgctggaccttccat	o
711 gctagacgttaggctga	o
712 gctacttagcgtga	o
713 gctaccttagcgtga	o
714 atcgactctcgagcgttctc	o
715 atgcactctcgagcgttctc	o
716 agtgactctccagcgttctc	o
717 gccagatgttagctgga	o
718 atcgactcgagcgttctc	o
719 atcgatcgagcgttctc	o
720 bgagaacgctcgaccttcgat	o
721 gctagacgttagcgtgga	sos
722 atcgactctcgagcgttctc	sos
723 tagacgttagcgtga	o
724 cgactctcgagcgttctc	o
725 ggggtcgaccttgagggggg	sos
726 gctaacgttagcgtga	o
727 cgtcgtcgt	o
728 gagaa:gctggaccttccat	o
729 atcgacctacgtgcgttztc	o
730 atzgacctacgtgcgttctc	o
731 gctagazgttagcgt	o
732 atcgactctcgagzgttctc	o
733 ggggtaatgcatcagggggg	sos
734 ggctgtattcctgactgcc	s
735 ccatgctaacctctagc	o
736 gctagatgttagcgtga	o
737 cgtaccttacggtga	o
738 tccatgctggtcctgatgct	o
739 atcgactctctcgagcgttctc	o
740 gctagagcttagcgtga	o
741 atcgactctcgagtgttctc	o
742 aacgctcgaccttcgat	o
743 ctcaacgctggaccttccat	o
744 atcgacctacgtgcgttctc	o
745 gagaatgctggaccttccat	o
746 tcacgctaacctctgac	o
747 bgagaacgctccagcactgat	o
748 bgagcaagctggaccttccat	o
749 cgctagaggttagcgtga	o
750 gctagatgttaacgt	o
751 atggaaaggtccacgttctc	o
752 gctagatgttagcgt	o
753 gctagacgttagtgt	o
754 tccatgacggtcctgatgct	o
755 tccatggcggctcctgatgct	o
756 gctagacgatagcgt	o
757 gctagtcgatagcgt	o
758 tccatgacgttctgatgct	o
759 tccatgtcgttctgatgct	o
760 gctagacgttagzgt	o
761 gctaggcgttagcgt	o
762 tccatgtzggctcctgatgct	o
763 tccatgtcggctcctgatgct	o
764 atzgactctzgagzgttctc	o
765 atggaaaggtccagtggttctc	o
766 gcatgacgttagcgt	o

TABLE 1-continued

SEQ ID NO: ODN SEQUENCE	BACKBONE
767 ggggtcaacgttgagggggg	s
768 ggggtcaagctctgagggggg	sos
769 cgcgcgcgcgcgcgcgcgcg	o
770 cccccccccccccccccccccccc	s
771 cccccccccccccccccccccccc	s
772 tcaatgtcgctcctgatcct	o
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774 tccatgtcgatcctgatgct	o
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TABLE 1-continued

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TABLE 1-continued

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TABLE 1-continued

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1062 tgggtcttttgggtccttgtct	s



not exclusively associated with atopic or allergic symptoms. An "initiator" as used herein refers to a composition or environmental condition which triggers asthma. Initiators include, but are not limited to, allergens, cold temperatures, exercise, viral infections, SO<sub>2</sub>.

[0103] In another aspect the invention provides methods for treating or preventing asthma or allergy in a hypo-responsive subject. As used herein, a hypo-responsive subject is one who has previously failed to respond to a treatment directed at treating or preventing asthma or allergy or one who is at risk of not responding to such a treatment. The treatment directed at treating or preventing asthma or allergy may be an asthma/allergy medicament, in which case the hypo-responsive subject is one who is hypo-responsive to an asthma/allergy medicament.

[0104] Other subjects who are hypo-responsive include those who are refractory to an asthma/allergy medicament. As used herein, the term "refractory" means resistant or failure to yield to treatment. Such subjects may be those who never responded to an asthma/allergy medicament (i.e., subjects who are non-responders), or alternatively, they may be those who at one time responded to an asthma/allergy medicament, but have since that time have become refractory to the medicament. In some embodiments, the subject is one who is refractory to a subset of medicaments. A subset of medicaments is at least one medicament. In some embodiments, a subset refers to 2, 3, 4, 5, 6, 7, 8, 9, or 10 medicaments.

[0105] In other embodiments, hypo-responsive subjects are elderly subjects, regardless of whether they have or have not previously responded to a treatment directed at treating or preventing asthma or allergy. Elderly subjects, even those who have previously responded to such treatment, are considered to be at risk of not responding to a future administration of this treatment. Similarly, neonatal subjects are also considered to be at risk of not responding to treatment directed at treating or preventing asthma or allergy.

[0106] In some embodiments, an immunostimulatory nucleic acid is administered to the hypo-responsive subject without the further administration of an asthma/allergy medicament. In yet other embodiments, an asthma/allergy medicament is administered to the hypo-responsive subject, in which case it may be administered substantially simultaneously (i.e., concurrently) with, or following the administration of the immunostimulatory nucleic acid.

[0107] An "asthma/allergy medicament" as used herein is a composition of matter which reduces the symptoms, inhibits the asthmatic or allergic reaction, or prevents the development of an allergic or asthmatic reaction. Various types of medicaments for the treatment of asthma and allergy are described in the Guidelines For The Diagnosis and Management of Asthma, Expert Panel Report 2, NIH Publication No. 97/4051, Jul. 19, 1997, the entire contents of which are incorporated herein by reference. The summary of the medicaments as described in the NIH publication is presented below.

[0108] In most embodiments the asthma/allergy medicament is useful to some degree for treating both asthma and allergy. Some asthma/allergy medicaments are preferably used in combination with the immunostimulatory nucleic acids to treat asthma. These are referred to as asthma

medicaments. Asthma medicaments include, but are not limited, PDE-4 inhibitors, bronchodilator/beta-2 agonists, K<sup>+</sup> channel openers, VLA-4 antagonists, neurokin antagonists, TXA<sub>2</sub> synthesis inhibitors, xanthanines, arachidonic acid antagonists, 5 lipoxygenase inhibitors, thromboxan A<sub>2</sub> receptor antagonists, thromboxane A<sub>2</sub> antagonists, inhibitor of 5-lipoxygenase activation proteins, and protease inhibitors.

[0109] Bronchodilator/beta-2 agonists are a class of compounds which cause bronchodilation or smooth muscle relaxation. Bronchodilator/beta-2 agonists include, but are not limited to, salmeterol, salbutamol, albuterol, terbutaline, D2522/formoterol, fenoterol, bitolterol, pirbuterol methylxanthines and orciprenaline. Long-acting  $\beta_2$  agonists and bronchodilators which are used for long-term prevention of symptoms in addition to the anti-inflammatory therapies. They function by causing bronchodilation, or smooth muscle relaxation, following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction. These compounds also inhibit mast cell mediator release, decrease vascular permeability and increase mucociliary clearance. Long-acting  $\beta_2$  agonists include, but are not limited to, salmeterol and albuterol. These compounds are usually used in combination with corticosteroids and generally are not used without any inflammatory therapy. They have been associated with side effects such as tachycardia, skeletal muscle tremor, hypokalemia, and prolongation of QTc interval in overdose.

[0110] Methylxanthines, including for instance theophylline, have been used for long-term control and prevention of symptoms. These compounds cause bronchodilation resulting from phosphodiesterase inhibition and likely adenosine antagonism. It is also believed that these compounds may effect eosinophilic infiltration into bronchial mucosa and decrease T-lymphocyte numbers in the epithelium. Dose-related acute toxicities are a particular problem with these types of compounds. As a result, routine serum concentration must be monitored in order to account for the toxicity and narrow therapeutic range arising from individual differences in metabolic clearance. Side effects include tachycardia, nausea and vomiting, tachyarrhythmias, central nervous system stimulation, headache, seizures, hematemesis, hyperglycemia and hypokalemia. Short-acting  $\beta_2$  agonists/bronchodilators relax airway smooth muscle, causing the increase in air flow. These types of compounds are a preferred drug for the treatment of acute asthmatic systems. Previously, short-acting  $\beta_2$  agonists had been prescribed on a regularly-scheduled basis in order to improve overall asthma symptoms. Later reports, however, suggested that regular use of this class of drugs produced significant diminution in asthma control and pulmonary function (Sears, et al. *Lancet*; 336:1391-6, 1990). Other studies showed that regular use of some types of  $\beta_2$  agonists produced no harmful effects over a four-month period but also produced no demonstrable effects (Drazen, et al., *N. Eng. J. Med.*; 335:841-7, 1996). As a result of these studies, the daily use of short-acting  $\beta_2$  agonists is not generally recommended. Short-acting  $\beta_2$  agonists include, but are not limited to, albuterol, bitolterol, pirbuterol, and terbutaline. Some of the adverse effects associated with the administration of short-acting  $\beta_2$  agonists include tachycardia, skeletal muscle tremor, hypokalemia, increased lactic acid, headache, and hyperglycemia.

agents such as adjuvants to enhance immune responses even further. The immunostimulatory nucleic acid, asthma/allergy medicament and other therapeutic agent may be administered simultaneously or sequentially. When the other therapeutic agents are administered simultaneously they can be administered in the same or separate formulations, but are administered at the same time. The other therapeutic agents are administered sequentially with one another and with the immunostimulatory nucleic acid and asthma/allergy medicament, when the administration of the other therapeutic agents and the immunostimulatory nucleic acid and asthma/allergy medicament is temporally separated. The separation in time between the administration of these compounds may be a matter of minutes or it may be longer. Other therapeutic agents include but are not limited to non-nucleic acid adjuvants, cytokines, antibodies, antigens, etc.

[0160] A "non-nucleic acid adjuvant" is any molecule or compound except for the immunostimulatory nucleic acids described herein which can stimulate the humoral and/or cellular immune response. Non-nucleic acid adjuvants include, for instance, adjuvants that create a depo effect, immune stimulating adjuvants, adjuvants that create a depo effect and stimulate the immune system and mucosal adjuvants.

[0161] An "adjuvant that creates a depo effect" as used herein is an adjuvant that causes an antigen or allergen to be slowly released in the body, thus prolonging the exposure of immune cells to the antigen or allergen. This class of adjuvants includes but is not limited to alum (e.g., aluminum hydroxide, aluminum phosphate); or emulsion-based formulations including mineral oil, non-mineral oil, water-in-oil or oil-in-water-in oil emulsion, oil-in-water emulsions such as Seppic ISA series of Montanide adjuvants (e.g., Montanide ISA 720, AirLiquide, Paris, France); MF-59 (a squalene-in-water emulsion stabilized with Span 85 and Tween 80; Chiron Corporation, Emeryville, Calif.; and PROVAX (an oil-in-water emulsion containing a stabilizing detergent and a micelle-forming agent; IDEC, Pharmaceuticals Corporation, San Diego, Calif.).

[0162] An "immune stimulating adjuvant" is an adjuvant that causes activation of a cell of the immune system. It may, for instance, cause an immune cell to produce and secrete cytokines. This class of adjuvants includes but is not limited to saponins purified from the bark of the *Q. saponaria* tree, such as QS21 (a glycolipid that elutes in the 21<sup>st</sup> peak with HPLC fractionation; Aquila Biopharmaceuticals, Inc., Worcester, Mass.); poly[di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research Institute, USA); derivatives of lipopolysaccharides such as monophosphoryl lipid A (MPL; Ribi ImmunoChem Research, Inc., Hamilton, Mont.), muramyl dipeptide (MDP; Ribi) and threonyl-muramyl dipeptide (t-MDP; Ribi); OM-174 (a glucosamine disaccharide related to lipid A; OM Pharma SA, Meyrin, Switzerland); and Leishmania elongation factor (a purified Leishmania protein; Corixa Corporation, Seattle, Wash.).

[0163] "Adjuvants that create a depo effect and stimulate the immune system" are those compounds which have both of the above-identified functions. This class of adjuvants includes but is not limited to ISCOMS (Immunostimulating complexes which contain mixed saponins, lipids and form virus-sized particles with pores that can hold antigen; CSL, Melbourne, Australia); SB-AS2 (SmithKline Beecham adju-

vant system #2 which is an oil-in-water emulsion containing MPL and QS21; SmithKline Beecham Biologicals [SBB], Rixensart, Belgium); SB-AS4 (SmithKline Beecham adjuvant system #4 which contains alum and MPL; SBB, Belgium); non-ionic block copolymers that form micelles such as CRL 1005 (these contain a linear chain of hydrophobic polyoxpropylene flanked by chains of polyoxyethylene; Vaxcel, Inc., Norcross, Ga.); and Syntex Adjuvant Formulation (SAF, an oil-in-water emulsion containing Tween 80 and a nonionic block copolymer; Syntex Chemicals, Inc., Boulder, Colo.).

[0164] A "non-nucleic acid mucosal adjuvant" as used herein is an adjuvant other than an immunostimulatory nucleic acid that is capable of inducing a mucosal immune response in a subject when administered to a mucosal surface in conjunction with an antigen or allergen. Mucosal adjuvants include but are not limited to Bacterial toxins: e.g., Cholera toxin (CT), CT derivatives including but not limited to CT B subunit (CTB) (Wu et al., 1998, Tochikubo et al., 1998); CTD53 (Val to Asp) (Fontana et al., 1995); CTK97 (Val to Lys) (Fontana et al., 1995); CTK104 (Tyr to Lys) (Fontana et al., 1995); CTD53/K63 (Val to Asp, Ser to Lys) (Fontana et al., 1995); CTH54 (Arg to His) (Fontana et al., 1995); CTN107 (His to Asn) (Fontana et al., 1995); CTE114 (Ser to Glu) (Fontana et al., 1995); CTE112K (Glu to Lys) (Yamamoto et al., 1997a); CTS61F (Ser to Phe) (Yamamoto et al., 1997a, 1997b); CTS106 (Pro to Lys) (Douce et al., 1997, Fontana et al., 1995); and CTK63 (Ser to Lys) (Douce et al., 1997, Fontana et al., 1995), Zonula occludens toxin, zot, *Escherichia coli* heat-labile enterotoxin, Labile Toxin (LT), LT derivatives including but not limited to LT B subunit (LTB) (Verweij et al., 1998); LT7K (Arg to Lys) (Komase et al., 1998, Douce et al., 1995); LT61F (Ser to Phe) (Komase et al., 1998); LT112K (Glu to Lys) (Komase et al., 1998); LT118E (Gly to Glu) (Komase et al., 1998); LT146E (Arg to Glu) (Komase et al., 1998); LT192G (Arg to Gly) (Komase et al., 1998); LTK63 (Ser to Lys) (Marchetti et al., 1998, Douce et al., 1997, 1998, Di Tommaso et al., 1996); and LTR72 (Ala to Arg) (Giuliani et al., 1998), Pertussis toxin, PT. (Lycke et al., 1992, Spangler BD, 1992, Freytag and Clements, 1999, Roberts et al., 1995, Wilson et al., 1995) including PT-9K/129G (Roberts et al., 1995, Cropley et al., 1995); Toxin derivatives (see below) (Holmgren et al., 1993, Verweij et al., 1998, Rappuoli et al., 1995, Freytag and Clements, 1999); Lipid A derivatives (e.g., monophosphoryl lipid A, MPL) (Sasaki et al., 1998, Vancott et al., 1998; Muramyl Dipeptide (MDP) derivatives (Fukushima et al., 1996, Ogawa et al., 1989, Michalek et al., 1983, Morisaki et al., 1983); Bacterial outer membrane proteins (e.g., outer surface protein A (OspA) lipoprotein of *Borrelia burgdorferi*, outer membrane protein of *Neisseria meningitidis*) (Marinero et al., 1999, Van de Verg et al., 1996); Oil-in-water emulsions (e.g., MF59) (Barchfield et al., 1999, Verschoor et al., 1999, O'Hagan, 1998); Aluminum salts (Isaka et al., 1998, 1999); and Saponins (e.g., QS21) Aquila Biopharmaceuticals, Inc., Worcester, Mass.) (Sasaki et al., 1998, MacNeal et al., 1998), ISCOMS, MF-59 (a squalene-in-water emulsion stabilized with Span 85 and Tween 80; Chiron Corporation, Emeryville, Calif.); the Seppic ISA series of Montanide adjuvants (e.g., Montanide ISA 720; AirLiquide, Paris, France); PROVAX (an oil-in-water emulsion containing a stabilizing detergent and a micelle-forming agent; IDEC Pharmaceuticals Corporation, San Diego, Calif.); Syntex Adjuvant Formulation (SAF;

Syntex Chemicals, Inc., Boulder, Colo.); poly[di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research Institute, USA) and Leishmania elongation factor (Corixa Corporation, Seattle, Wash.).

[0165] Immune responses can also be induced or augmented by the co-administration or co-linear expression of cytokines (Bueller & Mulligan, 1996; Chow et al., 1997; Geissler et al., 1997; Iwasaki et al., 1997; Kim et al., 1997) or B-7 co-stimulatory molecules (Iwasaki et al., 1997; Tsuji et al., 1997) with the immunostimulatory nucleic acids and asthma/allergy medicaments. The cytokines can be administered directly with immunostimulatory nucleic acids or may be administered in the form of a nucleic acid vector that encodes the cytokine, such that the cytokine can be expressed *in vivo*. In one embodiment, the cytokine is administered in the form of a plasmid expression vector. The term "cytokine" is used as a generic name for a diverse group of soluble proteins and peptides which act as humoral regulators at nano- to picomolar concentrations and which, either under normal or pathological conditions, modulate the functional activities of individual cells and tissues. These proteins also mediate interactions between cells directly and regulate processes taking place in the extracellular environment. Examples of cytokines include, but are not limited to IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18 granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), interferon- $\gamma$  (IFN- $\gamma$ ), IFN- $\alpha$ , tumor necrosis factor (TNF), TGF- $\beta$ , FLT-3 ligand, and CD40 ligand. Cytokines play a role in directing the T cell response. Helper (CD4+) T cells orchestrate the immune response of mammals through production of soluble factors that act on other immune system cells, including other T cells. Most mature CD4+ T helper cells express one of two cytokine profiles: Th1 or Th2. In some embodiments it is preferred that the cytokine be a Th1 cytokine.

[0166] The term "effective amount" of an immunostimulatory nucleic acid and an asthma/allergy medicament refers to the amount necessary or sufficient to realize a desired biologic effect. For example, an effective amount of an immunostimulatory nucleic acid and an asthma/allergy medicament for treating or preventing asthma or preventing is that amount necessary to prevent the development of IgE in response to an allergen or initiator upon exposure to the allergen or initiator is that amount necessary to cause the shift from Th2 to Th1 response in response to an allergen or initiator.

[0167] Combined with the teachings provided herein, by choosing among the various active compounds and weighing factors such as potency, relative bioavailability, patient body weight, severity of adverse side-effects and preferred mode of administration, an effective prophylactic or therapeutic treatment regimen can be planned which does not cause substantial toxicity and yet is entirely effective to treat the particular subject. The effective amount for any particular application can vary depending on such factors as the disease or condition being treated, the particular immunostimulatory nucleic acid or asthma/allergy medicament being administered (e.g. the type of nucleic acid, i.e. a CpG nucleic acid, the number of unmethylated CpG motifs or their location in the nucleic acid, the degree of modification of the backbone to the oligonucleotide the type of medicament), the size of the subject, or the severity of the disease

or condition. One of ordinary skill in the art can empirically determine the effective amount of a particular immunostimulatory nucleic acid and/or asthma/allergy medicament and/or other therapeutic agent without necessitating undue experimentation.

[0168] Depending upon the aspect of the invention, the immunostimulatory nucleic acid and asthma/allergy medicament may be administered in a synergistic amount effective to treat or prevent asthma or allergy. A synergistic amount is that amount which produces a physiological response that is greater than the sum of the individual effects of either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. For instance, in some embodiments of the invention, the physiological effect is a reduction in IgE levels. A synergistic amount is that amount which produces a reduction in IgE that is greater than the sum of the IgE reduced by either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. In other embodiments, the physiological result is a shift from Th2 cytokines, such as IL-4 and IL-5, to Th1 cytokines, such as IFN- $\gamma$  and IL-12. The synergistic amount in this case is that amount which produces the shift to a Th1 cytokine that is greater than the sum of the shift produced by either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. In other embodiments the physiological result is a decrease in eosinophilia, hyperreactivity, or lung function.

[0169] In some embodiments of the invention, the immunostimulatory nucleic acid is administered in an effective amount for preventing bacterial or viral infection. Immunostimulatory nucleic acids are known to be useful for preventing bacterial and viral infections. Bacterial and viral infections exacerbate and/or induce allergy and/or asthma. In this aspect of the invention, the immunostimulatory nucleic acid is administered to the subject in an amount effective to prevent bacterial and viral infection and the asthma/allergy medicament is administered to the subject when symptoms of allergy or asthma appear. Thus, the immunostimulatory nucleic acid is administered to the subject and then the asthma/allergy medicament is subsequently administered to the subject or they are administered together at the same time. This method is particularly useful in subjects such as children and immunocompromised subjects, or elderly subjects, who are particularly susceptible to bacterial or viral disease.

[0170] In aspects of the invention directed at treating subjects in anticipation of an asthmatic or allergic event or season (e.g., in anticipation of the hay-fever season), the subjects may be administered an immunostimulatory nucleic acid in an effective amount for preventing the asthma or allergy. In related embodiments of this method, an asthma/allergy medicament is also administered to the subject. In these latter instances, the amount of the immunostimulatory nucleic acid administered may be that amount necessary to reduce the effective dose of the asthma/allergy medicament which is required to treat or prevent the asthma or allergy.

[0171] Thus, in these embodiments, the immunostimulatory nucleic acid potentiates the effect of the asthma/allergy medicament. The ability to potentiate the effect of an asthma/allergy medicament is useful since it allows for a reduction in the administered dose of an asthma/allergy medicament with the same or better therapeutic result. As an